Brain-gut axis as an example of the bio-psycho-social model

I Wilhelmsen

In research we often apply hypothesis testing which assumes a linear, causal relationship between two or more factors. This is a valid way of testing fragments of a complicated chaos of known and unknown elements. However, I want us to reflect upon the thought that the answers we get are limited by the questions we ask. It is said that "If you have a hammer, the only thing you see are nails". Western medical education and research has, for more than a century, been dominated by a dualistic view of human nature, and from the psychoanalytical tradition (based on Freud's work) we have learned to differentiate between biological (physical, organic, somatic) on one side and psychological (thoughts and emotions) on the other. This dualistic view, emphasising that psychological and biological are two entirely different aspects of human life, is mechanistic and reductionistic, and in today's world a non-scientific position to hold.[1] In spite of many decades of research, there is no evidence that emotions can "pile up" somewhere in the body and that psychological conflicts, if unresolved, are converted to somatic symptoms or diseases. On the contrary, science is moving into a position of integration, and the cognitive science (such as neuroscience) has developed rapidly in recent years. You cannot experience an emotion or think a thought without biological correlates. Unresolved mental conflicts lead to activation of the central nervous system (CNS), and of the autonomic systems. Activation theories, such as the "cognitive activation theory of stress" states that the stress response is the same as activation—a general alarm system operating whenever the organism registers that there is a discrepancy between what is expected and what really exists.[2] The brain-gut axis is a good example of a circular relationship between different factors, and illustrates that research on interrelationship and interaction is necessary to understand the whole picture (fig 1). Chronic functional gastrointestinal symptoms can be seen as a result of dysregulation of intestinal motor, sensory, and CNS activity.

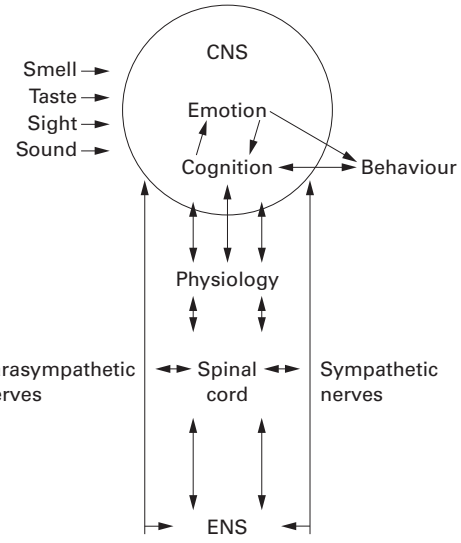

Figure 1 Brain-gut axis (with emphasis on the central nervous system (CNS) psychological process). ENS, enteric nervous system.

Cognitions, defined as verbal or pictorial events in our stream of consciousness, are often divided into three aspects: *cognitive events* are thoughts that go through our minds, *cognitive processes* are evaluations, opinions, abstractions, more elaborated reflections, and values, and *cognitive schemata* are often called basic assumptions or life rules. Our schemata are developed from previous experiences, and are activated in specific situations. The relationship between cognition and emotion is illustrated when you experience something threatening or dangerous. Our inner dialogue is dominated by automatic thoughts, based on our basic assumptions. This interpretation of the situation (cognition) is immediately followed by the emotion of anxiety (often called fear). All emotions have physiological correlates; in anxiety, sympathetic, and to a lesser degree parasympathetic, activation leads to tachycardia, hyperventilation, sweating, nausea, need to defecate, etc. Anxiety is a biological warning system to react mentally and bodily to threatening or dangerous situations. Attention is directed towards the threat, and the body prepares for fight, flight or freeze, necessary for survival. We experience this biological reaction every time we interpret a situation or a physical symptom as threatening or dangerous. The body does not control whether our interpretation is, in fact, correct. Imagined danger is just as anxiety provoking as real danger. A person with basic cognitions such as "The world is unsafe", "Physical symptoms are not normal and always a sign of serious disease" or "I will soon die of cancer" will screen the world and body for signs of threat, and hence experience more anxiety reactions than if they did not have these cognitions (termed "catastrophising").

The terminology in human research reflects the fact that there is great variance and individual differences. In animal research there is more clarity and consensus in terminology. Words such as emotion or "feeling" have different meanings. There are two main theories underlining different aspects of emo-

Department of Internal Medicine, Deaconness Home Hospital, University of Bergen, 5009 Bergen, Norway

Correspondence to:
Professor I Wilhelmsen.
Ingvard.wilhelmsen@meda.uib.no

Abbreviations used in this paper: CNS, central nervous system.

tions: emotions are primarily brain events with physiological concomitants—the efferent link; on the other hand, an essential part of emotions is feedback from peripheral physiological activation—the afferent link.[3] Different labels are attached to emotions. The most commonly used are glad, sad, anxious, mad, surprised, confused, and jealous. Shame and disgust are also defined by some as basic emotions.

A central aspect of functional gastrointestinal disorders is pain. Pain is often defined as an unpleasant sensory and emotional experience, associated with actual or potential tissue damage, or described in terms of such damage. Nociception refers to the reception of signals in the CNS, evoked by activation of specialised sensory receptors (nociceptors) that provide information about tissue damage. The brain-gut axis is bidirectional and integrative. There is input from sensory sources (sight, smell, etc) and somatosensory/viscerosensory sources, modified by cognitions and affect, and a neural circuit in the CNS, the spinal cord, autonomic nervous system, and enteric nervous system.

Anxiety is seen as an important modulating factor in the perception of pain: increased anxiety is associated with increased pain reports. Adrenaline is released at sympathetic nerve endings which may sensitise nociceptors, and triggers somatic reflexes by increasing muscle tension. However, anxiety and pain may be methodologically confounded as they both lead to a general sympathetic physiological arousal and share common response patterns. During threatening situations, endogenous opioids are released, contributing to an analgesic effect. The picture is complicated: anxiety for pain leads to attention towards pain and may increase it, while anxiety for something else leads to distraction from pain, thereby decreasing it. This may be an explanation for the finding that patients with irritable bowel syndrome are sensitive to distension in the gut but are not fearful of sensations from other areas, and hence are less sensitive than normal controls to painful stimulation of the skin.[4] Attention, defined by William James as "withdrawal from some things in order to deal effectively with others", is like a selective filter, an important factor in pain perception, and incorporated in several theories of pain.[3 5] Patients with anxiety disorders frequently have somatic complaints. Constitutional predisposition (biological vulnerability) and psychological factors probably determine whether the patient has primarily muscular, cardiovascular, or gastrointestinal symptoms.[6]

Sensitisation and somatisation

In functional gastrointestinal disorders, subjective health complaints, such as nausea, discomfort, and pain are the major targets for treatment. Perception of somatic stimuli is probably different for different patients. *Sensitisation* is defined as increased reactivity to stimuli in pain pathways, and *visceral hypersensitivity* is the exaggerated experience of pain in response to mildly painful or even normal visceral stimuli. Nociceptors are activated, and the threshold decreased in the injured part (primary hyperalgesia) and surrounding tissue (secondary hyperalgesia). This increased responsiveness of nociceptors is called sensitisation. Only spinal afferents appear to be involved in the transmission of visceral pain. It is specific to the bowel, and not similar to somatic pain. The opposite of sensitisation is *habituation*, decreased efficiency due to repeated use. Usually there is no habituation to painful stimuli. Sensitisation may occur in the dorsal horn of the spinal cord but possibly also at the level of the limbic structures.[7] The mechanism may be that of kindling, a decreased threshold for electric after-discharge produced by electrical or chemical stimulation of limbic structures (amygdala, hippocampus). The word *somatisation* is used in modern diagnostic systems such as ICD-10 and DSM-IV. Freud defined the word as a way to express emotions or psychological conflicts, but today the word is a descriptive term meaning somatic complaints not fully explained by any known medical condition. The patient with somatisation has a tendency to notice many bodily sensations and to interpret them as symptoms of organic disease. To obtain a diagnosis of somatisation disorder there must be pain in four different sites or functions: gastrointestinal complaints, sexual dysfunction, muscle skeletal symptoms, and a pseudoneurological complaint (dizziness, vertigo, seizures, etc). Subjective health complaints are very common in the normal population, especially exhaustion, fatigue, muscle pain, and gastrointestinal complaints.[8] Some people seem to be more sensitive than others to these normal complaints. These patients have a sensitive mind in a sensitive body. Sensitisation has been suggested as the underlying mechanism for somatisation, and this can occur at different levels of the brain-gut axis. In addition to the mechanisms in the CNS, the model also assumes that psychological factors influence the synaptic mechanisms and feed forward loops from the brain. These central pathways, descending from the brain, modulate the transmission of nociceptive information at the spinal cord level. Melzak and Wall have pointed out the possibility that affective and cognitive factors, such as anxiety, attention, and expectation can influence pain via these descending pathways.[9]

Patients with somatisation are diagnosed differently in different countries and by different specialists. Common diagnoses are chronic fatigue syndrome, multiple chemical sensitivity, food intolerance, functional dyspepsia, irritable bowel syndrome, fibromyalgia, etc. These conditions should not be seen as psychological problems. Whether symptoms are seen as extraintestinal disturbances of functional gastrointestinal disorders or extramuscular disturbances of fibromyalgia depends on different factors. In our own studies we have found that somatisation differentiates between functional and organic gastrointestinal disorders.[10] Some people probably have a sensitive mind and a sensitive body, some a sensitive body and a normal mind, and some a sensitive mind in a normal body. In functional gastrointestinal dis-

orders, sensitisation of specific neurones may be important, and in the brain-gut axis treatment may be aimed at any point where it is possible to influence the individual. This can be a combination of somatic and psychological approaches, including drugs, physical training, and psychotherapy.

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